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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
09/28/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IP.Docketing@aporter.com

Office Action Summary	Application No.	Applicant(s)	
	10/587,644	TOSCANO ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *2-14,17-42 and 44-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,15,16 and 43* is/are rejected.

7)☒ Claim(s) *15 and 16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/27/2006; 3/26/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group IX, claims 1, 3-4, 11, 15-16, 42-44, 46 and 49-52 (in part) in the reply filed on 7/16/2010 is acknowledged.

2. Applicant's election without traverse of the compound of formula (I) wherein m and n are each 0, and R^1 and R^2 are each $-CH_2CF_3$, with the identificatiobn that at least claims 1, 15-16 and 43 read on the elected specie in the reply filed on 7/16/2010 is acknowledged.

3. Claims 2, 5-10, 12-14, 17-41, 45 and 47-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/16/2010.

4. Claims 3-4, 11, 42, 44, 46 and 49-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected specie, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/16/2010.

Claim Objections

5. Claims 15-16 are objected to because of the following informalities: the claims recite "each R1" in the first lines; however, there is only one R1 recited in the compound of claim 1; it is recommended that the word "each" be removed from the claims to overcome this objection. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 15-16 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites a compound of formula (I); however, the depicted formula (I) has a net charge of -1, i.e., formula (I) depicts an ion. Since compounds normally are comprised of molecules that have a neutral charge, the subject matter of the recited "compound of formula (I)" is confusing. For the purpose of identifying prior art it is assumed that any ion or salt that contains the depicted ion of formula (I) is within the scope of the recited "compound of formula (I)".

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The generic terms recited in the instant claims of "hydrates" and "solvates" of the compounds of formula (I) and of the elected compound are not considered to have

sufficient description in the specification to demonstrate applicant was in possession at the time of filing of each of these genus terms with respect to the elected compound. Although the specification does have a cursory disclosure at p. 27, lines 4-6, mentioning what is meant by hydrate, i.e., that a hydrate means a compound of the present invention that further includes a stoichiometric or non-stoichiometric amount of water bound by non-covalent intermolecular forces. The prior art illustrates that preparation of solvates and hydrates is not predictable, but requires trial and error experimentation to identify each such hydrate or solvate of any given compound. Therefore, the brief discussion at the indicated location is not considered to demonstrate that applicant was in possession of, nor does it place the public in possession of the generic terms of "hydrates" or "solvates" of the elected compound.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a compound of formula (I), or a pharmaceutically acceptable salt, solvate or hydrate thereof.

(1) Level of skill and knowledge in the art:

The level of skill in the art is high. However, preparation of hydrates and solvates of a given compound, when none are yet known for that compound, is unpredictable.

Vippagunta et al. ("Crystalline solids"; 2001; Advanced Drug Delivery Reviews; 48: 3-26) teaches many drugs exist in the crystalline solid state due to reasons of stability and ease of handling during the various stages of drug development; crystalline solids can exist in the form of polymorphs, solvates or hydrates; phase transitions such as polymorph interconversion, desolvation of solvate, formation of hydrate and conversion of crystalline to amorphous form may occur during various pharmaceutical processes, which may alter the dissolution rate and transport characteristics of the drug;

hence it is desirable to choose the most suitable and stable form of the drug in the initial stages of drug development (abstract); predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult; each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compound; certain molecular shapes and features favor the formation of crystals without solvent, these compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents (p. 18, section 3.4). This article illustrates that for a given compound it is unpredictable whether solvates or hydrates will even form, let alone which solvates or hydrates; and that determination of such solvates and hydrates requires extensive manpower and effort to characterize.

(2) Partial structure:

The general formula (I) is disclosed, although it might be argued the elected compound is not specifically disclosed, except when specific choices are selected from within a broad generic Markush structure from the priority documents' disclosures.

The specification discusses that that a hydrate means a compound of the present invention that further includes a stoichiometric or non-stoichiometric amount of water bound by non-covalent intermolecular forces. Hydrates are generally present in crystalline form. A solvate would have some solvent molecule and compound present, typically in small whole number ratios, in a crystalline form.

(3) Physical and/or chemical properties and (4) Functional characteristics:

A solvate is known to be a crystalline form where a fixed, small whole number ratio of solvent molecules and active compound are present in the crystalline form; a hydrate would have a small whole number ratio of water and compound molecules present in a crystalline form.

(5) Method of making the claimed invention:

No method of making any solvate or hydrate has been disclosed, let alone a representative number to demonstrate possession of the entire generic terms.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1-20 and 23-29 is/are broad and generic, with respect to all possible solvates and hydrates encompassed by the claims. The possible structural variations are limitless to any solvate and hydrate forms of the claimed compounds. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of the elected compound and compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

10. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for how to make some compounds of formula (I), does not reasonably provide enablement for how to make "solvates" or "hydrates" of the elected compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

It is known in the art that formation of hydrates and solvates from a given compound is unpredictable, even when hydrates or solvates of a similar compound are known. The process to identify hydrates and solvates requires extensive work to characterize hydrates and solvates, if they form at all. No disclosure of how to prepare any solvate or hydrate of the elected compound was found in the specification, let alone a description of how to make a sufficient number of different solvates and hydrates of the elected compound to demonstrate how to make the entire genus of solvates and

hydrates. Considering the lack of guidance and lack of working examples, in view of the unpredictability in the art, it would require undue experimentation to make the genus of hydrates and solvates of the elected compound.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a compound of formula (I), or a pharmaceutically acceptable salt, solvate or hydrate thereof. Thus, the claims taken together with the specification imply any hydrate or solvate of the compound is readily prepared just from the disclosure of that compound, even though the claims are broadly drawn to a huge number of different compounds, including hydrates and solvates of all of those compounds.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Vippagunta et al. ("Crystalline solids"; 2001; Advanced Drug Delivery Reviews; 48: 3-26) teaches many drugs exist in the crystalline solid state due to reasons of stability and ease of handling during the various stages of drug development; crystalline solids can exist in the form of polymorphs, solvates or hydrates; phase transitions such as polymorph interconversion, desolvation of solvate, formation of hydrate and conversion of crystalline to amorphous form may occur during various pharmaceutical processes, which may alter the dissolution rate and transport characteristics of the drug; hence it is desirable to choose the most suitable and stable form of the drug in the initial stages of drug development (abstract); predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult; each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compound; certain molecular shapes and features favor the formation of crystals without solvent, these compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents (p. 18, section 3.4). This article illustrates the complexity and difficulty of predicting whether solvates or hydrates of a given compound will even form, let alone which solvates or hydrates; and that determination of such solvates and hydrates requires extensive manpower and effort to characterize.

(5) The relative skill of those in the art:

The relative skill in the art is high; those working in the art typically have a Ph.D. or M.D. degree.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for how to make some compounds within the scope of general formula (I).

However, the specification does not provide anything more than a description of what is meant by a hydrate; no method of making any hydrate or solvate of the elected compound was found, let alone specifically how to make the full scope of each of the generic terms.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to the complexity and difficulty in predicting and making solvates and hydrates of any given compound, even uncertainty as to whether a solvate or hydrate will form; and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

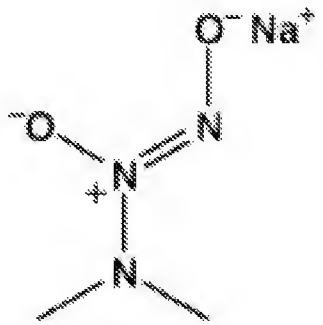
Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

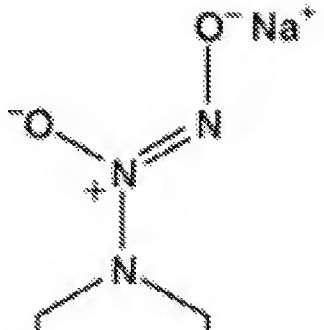
12. Claims 1, 15-16 and 43 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Fitzhugh et al. ("Qualitative Thin-Layer and High-Performance Liquid Chromatographic Analysis of 1-Substituted Diazen-1-ium-1,2-diolates on Aminopropyl-Bonded Silica Gel"; 2002; Analytical Biochemistry; 301: 97-102; IDS 3/26/2010 reference).

Fitzhugh teaches diazeniumdiolates, compounds containing the anionic $R_2N[N(O)NO]^-$ moiety, are receiving increasing use as nitric oxide (NO) donors in chemical and biochemical studies; the release of NO in such settings produces pharmacological effects including cytostasis, vasodilation, penile erection, etc.; these remarkable properties have generated considerable interest in the potential further use of diazeniumdiolates as therapeutic agents, particularly in the treatment of such important clinical disorders as pulmonary hypertension, cerebral vasospasm, impotence and thrombosis at blood-contact surfaces (p. 97, 1st paragraph). Compounds specifically taught include:



1

and



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(p. 99, Fig. 2). Compounds 1 and 2 are each salts of formula (I), i.e., a compound of formula (I), where n and m are 0, R^1 and R^2 are each alkyl (methyl for compound 1, ethyl for compound 2), reading on each of the instant claims.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 1, 14-15 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fitzhugh et al. ("Qualitative Thin-Layer and High-Performance Liquid Chromatographic Analysis of 1-Substituted Diazen-1-ium-1,2-diolates on Aminopropyl-Bonded Silica Gel"; 2002; Analytical Biochemistry; 301: 97-102; IDS 3/26/2010 reference BJ1); in view of Patani et al. ("Bioisosterism: A Rational Approach in Drug Design"; 1996; Chem. Rev.; 96: 3147-3176) and Ismail ("Important fluorinated drugs in experimental and clinical use"; 2002; Journal of Fluorine Chemistry; 118: 27-33).

The teachings of Fitzhugh have been outlined above. Fitzhugh does not specifically teach the elected compound, although this compound would be within the scope of the genus of diazeniumdiolates, compounds containing the anionic $R_2N[N(O)NO]^-$ moiety, taught by Fitzhugh.

Patani teaches a lead compound with a desired pharmacological activity may have associated with it undesirable side effects, characteristics that limit its bioavailability, or structural features which adversely influence its metabolism and excretion from the body; bioisosterism represents one approach used by the medicinal chemist for the rational modification of lead compounds into safer and more clinically effective agents (p. 3147, 1st paragraph); the ability of a group of bioisosteres to elicit similar biological activity has been attributed to common physicochemical properties, such as electronegativity, steric size and lipophilicity; values are correlated to biological activity (p. 3148, 2nd paragraph). Classical bioisosteres include the substitution of hydrogen by fluorine, which is one of the more commonly employed monovalent isosteric replacemic; steric parameters for hydrogen and fluorine are similar, the

difference in the electronic effects is often the basis for the major differences in the pharmacological properties of agents where fluorine has been substituted for hydrogen (p. 3149, 5th paragraph). This reference provides motivation to substitute F for H in an active compound in an attempt to find a safer and/or more effective agent than the starting compound.

Ismail teaches fluorine imparts desirable characteristics to drugs by modulating both the pharmacokinetics and pharmacodynamic properties of a drug; incorporation of fluorine into a drug increases the lipophilicity enhancing absorption into biological membranes whereby its small covalent radius can facilitate docking with their drug receptor(s) (abstract); bioisosteric substitution of hydrogen by fluorine is, therefore, an important strategy for incorporation of a group capable of reinforcing drug-receptor interactions, aiding translocation across lipid bilayers or absorption (p. 27, 2nd paragraph). Specific groups taught in molecules include trifluoromethyl groups (p. 28, right, 2nd paragraph; see also examples in compounds (8), which has two trifluoromethyl moieties and (9) (p. 28). This reference provides motivation to utilize trifluoromethyl groups in active compounds for the purposes taught by Ismail.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the terminal methyl hydrogens of the ethyl moieties of compound 2 taught by Fitzhugh, with fluorine atoms to give trifluoromethyl moieties, where the R groups of the diazeniumdiolate compound corresponds to $-CH_2CF_3$, i.e., the instant elected compound. The motivation would have been the expectation of

increased lipophilicity enhancing absorption and/or improved translocation across membranes to a target location.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571) 272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1628